UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/407,327	09/28/99	LOWELL G	406462000102

HM22/0118

THOMAS G WISEMAN
MORRISON & FOERSTER LLP
2000 PENNSYLVANIA AVENUE NW
WASHINGTON DC 20006-1688

EXAMINER	
GRASER, J	
ART UNIT	**PAPER NUMBER**
1645	8

DATE MAILED: 01/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/407,327	Lowell
Examiner	**Group Art Unit**
Graser, Jennifer	1645

☒ Responsive to communication(s) filed on *Amendment A 6/13/00* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-4 and 6-16* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4 and 6-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted 6/13/00, Paper No. 7/A is made. Claims 1-4 and 6-16 are currently pending.

Claim Rejections - 35 USC § 112

2. Claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 are vague and indefinite because it is unclear how the compositions are "suitable for oral or intranasal administration". It does not appear the components of the composition has changed by this amendment.

Claim Rejections - 35 USC § 102

3. Claims 1, 4 and 6 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zollinger et al (US 4,707,543).

Zollinger discloses detoxified lipopolysaccharide-outer membrane protein complexes and capsular polysaccharide-outer membrane protein complexes wherein the lipopolysaccharide noncovalently bonded to the protein whereas capsular polysaccharides can either be noncovalently or covalently bonded to the protein to form a complex (col. 4, lines 15-29). It is disclosed that the complexes are generally derived from Gram-negative bacteria, *N.meningitidis* Group B and

Neisseria gonorrhoeae are exemplified. Zollinger et al exemplify the use of outer membrane proteins purified by detergent extraction and ammonium sulfate precipitation and are known as "proteosomes". See Example 1. The compositions were used as vaccines and given subcutaneously (col. 7, line 60-col. 8, line 30).

Response to Applicant's Arguments:

Applicants argue that since the instant claims have been amended to characterize that the immunogenic composition is suitable for oral or intranasal administration it overcomes the prior art. This has been fully and carefully considered but is not deemed persuasive. Claims 1 and 4-6 are drawn to compositions which are structurally identical to those disclosed by Zollinger et al. A recitation of the intended use of the claimed invention (i.e., suitable for oral or intranasal administration) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Claim Rejections - 35 USC § 103

4. Claims 2, 3 and 7-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zollinger et al (4,707,543) in view of Cohen et al. (J. Infect. Dis, 1988, 157(5): 1068-1071) and Black et al (J. Infect. Dis., 1987, 155(6): 1260-1265) in further view of Ruegg et al (J. Immunolog. Methods, 1990, 135: 101-109).

The teachings of Zollinger et al are set forth above. However, they do not particularly exemplify compositions and/or vaccines wherein the LPS is from *Shigella*, particularly *S.flexneri* or *S.sonnei.*

Cohen et al teaches that *S.flexneri* or *S.sonnei* are causative agents of shigellosis. The reference teaches that the levels of antibodies to LPS present in subjects before or at the onset of an outbreak of shigellosis were associated with significant protection against the disease (p. 1070, col. 2). The reference further discloses that preexisting levels of antibodies to LPS indicate group-specific protection against shigellosis and that a previous report showed that serotype- and serogroup-specific immunity was conferred by the O-polysaccharide chain of LPS (p. 1070, col. 2).

Black et al. disclose that they modified attenuated *Salmonella typhi* strain TY21A to express the form I O polysaccharide antigen of *S.sonnei* and administered it as a bivalent, live oral vaccine (abstract). Vaccines had serum and local intestinal immune responses to *S.sonnei* lipopolysaccharide and the presence of specific IgA or IgG antibody before challenge with pathogenic *S.sonnei* was correlated with protection from illness (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made that one could use LPS from *S.flexneri* or *S.sonnei* in the detoxified lipopolysaccharide-outer membrane protein complexes disclosed by Zollinger because Zollinger teaches that LPS from any Gram negative bacteria could be used in the complexes and Cohen and Black specifically teach that the LPS from *S.flexneri* or *S.sonnei* is responsible for protection from shigellosis. One

of ordinary skill in the art would have been further motivated to use the *Shigella* LPS-proteosome complex because Ruegg et al specifically disclose that proteosomes have an adjuvant-like effect when complexed with lipopeptides without the need of additional adjuvants and one of ordinary skill in the art would expect a multivalent preparation to enhance the immunogenic activity of an antigen and therefore enhance the immunity of the LPS. Black et al also disclose that the oral administration route is an effective route for the treatment of shigellosis as it can allow for the *Shigella* to cross the mucosa thereby bringing the organism into direct contact with lymphoid tissue which will stimulate a stronger protective response. The use of oral and/or intranasal administration of bacterial pathogens has long been known in the art as an effective means for stimulating a mucosal immune response which is extremely important in protection against infection and therefore it would have been obvious to administer the instant compositions orally or intranasally because the prior art references teach success with this route of administration.

Response to Applicant's arguments:

Applicants argue that since the instant claims have been amended to characterize that the immunogenic composition is suitable for oral or intranasal administration it overcomes the prior art. This has been fully and carefully considered but is not deemed persuasive. Claims 2 and 3 are drawn to compositions which are structurally identical to those disclosed by Zollinger et al. in view of Cohen, Black and in light of Ruegg. A recitation of the intended use of the claimed invention (i.e., suitable for oral or intranasal administration) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed

invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. With regard to the method claims, the use of oral and/or intranasal administration of bacterial pathogens has long been known in the art as an effective means for stimulating a mucosal immune response which is extremely important in protection against infection and therefore it would have been obvious to administer the instant compositions orally or intranasally particularly because Black teaches success with this route of administration.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-4 and 6-16 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,985,284. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims differ only in that they recite a "non-detoxified antigenic lipopolysaccharide" as opposed to just a "lipopolysaccharide". Further, the intended use of "suitable for oral or intranasal administration" in the instant composition claims is only an

intended use and does not result in a structural difference between the patented claims and the and the claims of the instant invention.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

J Graser 1/17/01

Jennifer Graser
Primary Examiner
Art Unit 1645